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Direktorin: Prof. Dr. med. vet. Anja Kipar

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Dr. med. vet. Monika Hilbe

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Therese Irene Schertenleib

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Therese Irene Schertenleib

Institut für Veterinärpathologie
ivpz@vetpath.uzh.ch

Correlation of clinical and pathological diagnoses in cats and dogs
Korrelation von klinischen mit pathologischen Diagnosen bei Katzen und Hunden

Der Vergleich der klinischen und pathologischen Diagnose ist Voraussetzung für die Qualitätskontrolle, wird aber in der Veterinärmedizin nur selten gemacht. Für je 1000, an der Universität Zürich, untersuchte und sezierte Hunde und Katzen wurden das Vorkommen und die Übereinstimmung der für den Tod verantwortlichen Diagnose retrospektiv untersucht und mögliche Einflussfaktoren evaluiert. Bei 5.8% der Katzen und 5.2% der Hunde wurde keine Diagnose gestellt; bei 2.6% bzw. 3.6% der Fälle wurde nur eine klinische und bei 17.8% bzw. 11.2% nur eine pathologische Diagnose gefunden. Von den 73.9% Katzen und 79.8% Hunden mit beiden Diagnosen, stimmten diese in 38.3% und 36.2% total und in 17.9% bzw. 16.0% gar nicht überein. Die verbleibenden Fälle (43.8% und 47.8%) wurden durch die Sektion in verschiedenem Ausmaß spezifiziert. Bei beiden Spezies hatten die Art des Todes, die klinische Abteilung die das Tier zur Sektion sendete und die Qualität der Sektionsanamnese sowie bei Hunden zusätzlich die Zeitdauer zwischen Tod und Sektion, einen Einfluss auf das Vorkommen der Diagnosen. Hingegen beeinflussten das primär betroffene Organsystem und die der Diagnose zugrunde liegende Pathophysiologie bei beiden Spezies die Übereinstimmung am meisten. Deshalb liefert die Sektion in der Tiermedizin auch in Zeiten stark verbesserter klinischer Diagnostik und diagnostischer Methoden wertvolle Information für die Qualitätskontrolle und Ausbildung.

Stichwörter: Katzen, Hunde, klinische Diagnose, pathologische Diagnose, Korrelation

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The comparison of clinical antemortem and pathological postmortem diagnoses is a prerequisite for quality control but is rarely done in veterinary medicine. In 1000 cats and 1000 dogs examined and necropsied at the University of Zurich, the occurrence and concurrence of clinical and pathological diagnoses linked to death were evaluated and potential factors influencing them were correlated retrospectively. In 5.8% cats and 5.2% dogs no diagnosis was made; in 2.6% and 3.8% of cases only a clinical, and in 17.8% and 11.2%, respectively, only a pathological diagnosis was available. Of the 73.9% of cats and 79.8% of dogs with both diagnoses present, 38.3% and 36.2% were in total agreement, whereas total disagreement was found in 17.9% and 16.0%, respectively. The remaining cases (43.8% and 47.8%) exhibited different levels of further diagnosis specification through necropsy. In both species manner of death, the clinical discipline sending the animal to necropsy and the quality of the necropsy request, as well as the timespan between death and necropsy in dogs, proved to influence the occurrence of diagnoses. By contrast, the organ system affected and the disease entity of a certain diagnosis were for both species the most influential factors in the concurrence of diagnoses. Therefore in veterinary medicine, even in times of improving diagnostic abilities, necropsy still reveals important information for quality control and education.

Keywords: cats, dogs, postmortem diagnosis, antemortem diagnosis, correlation

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Abstract

The comparison of clinical antemortem and pathological postmortem diagnoses is a prerequisite for quality control but is rarely done in veterinary medicine.
In 1000 cats and 1000 dogs examined and necropsied at the University of Zurich, the occurrence and concurrence of clinical and pathological diagnoses linked to death were evaluated and potential factors influencing them were correlated retrospectively. In 5.8% cats and 5.2% dogs no diagnosis was made; in 2.6% and 3.8% of cases only a clinical, and in 17.8% and 11.2%, respectively, only a pathological diagnosis was available. Of the 73.9% of cats and 79.8% of dogs with both diagnoses present, 38.3% and 36.2% were in total agreement, whereas total disagreement was found in 17.9% and 16.0%, respectively. The remaining cases (43.8% and 47.8%) exhibited different levels of further diagnosis specification through necropsy. In both species manner of death, the clinical discipline sending the animal to necropsy and the quality of the necropsy request, as well as the timespan between death and necropsy in dogs, proved to influence the occurrence of diagnoses. By contrast, the organ system affected and the disease entity of a certain diagnosis were for both species the most influential factors in the concurrence of diagnoses. Therefore in veterinary medicine, even in times of improving diagnostic abilities, necropsy still reveals important information for quality control and education.

Keywords

Antemortem diagnosis, Cats, Control quality, Correlation study, Dogs, Influencing factors, Medicine, veterinary, Postmortem diagnosis

Introduction

Throughout the development of medical science, autopsy has been an important tool in determining cause of death, evaluating incompletely known disorders, establishing pathogenesis, discovering new diseases and evaluating the effectiveness of a new therapy as well as in medical education.[33] In human medicine its value is still widely accepted, although between 1960 and 1980 critical voices were raised[14,33,35,50] and its rules of implementation differ between countries. In 1978 Roberts[49] summarized 58 papers to attest the value and importance of autopsy, and, years later, laymen,[62] pathologists[61,63] medical students[13] and physicians[9] all agree on the benefits of autopsies. Autopsy remains a vital tool in gaining knowledge about diseases,[17,27,36] and is a teaching tool in education[17] as well as a contributing tool to quality monitoring.[8,75] General practitioners indicate that autopsy results do indeed modify their future clinical practice.[36] For epidemiological purposes autopsy gives precise information about the causes of death and contributes to an accurate monitoring of disease prevalence.[57] In veterinary medicine, too, there are surveys stressing the relevance of postmortem examination as a crucial part of quality monitoring and education.[37,74] To obtain the utmost from autopsies, clinical and pathological diagnoses have to be compared,[3,34,75] followed by an analysis of the causes of discrepancies.[70] On the other hand, it should be kept in mind that autopsy is not a method for assessing the overall quality of medical care[34] and that autopsy itself has its limitations. It excludes all cases in which the patient recovers.[4] Furthermore, approximately 4-8% of autopsies will not reveal a decisive explanation of a patient's clinical symptoms[12] and the complex processes of macroscopic and microscopic observations and data interpretation may be subject to error.[4,55] Although the scope of necropsy as an assessment tool has its limitations, within these limits it remains very powerful.[34] When correctly exploited, autopsy records serve to identify systematic errors in diagnostic processes.[3]

Therefore, it is surprising that in human medicine autopsy rates have declined dramatically over the last few decades[15] and are still falling in the 21st century.[48,52] In the United States overall autopsy rates declined from approximately 19% in the 1970s to 8% in 2003.[45] Looking at hospital deaths only, the decline is from 30% - 40% before 1970 to less than 10% in 2005. While national averages reflect high

autopsy rates at some hospitals, at the majority of nonacademic institutions few or no autopsies are ever performed.[15,58] The same tendency is seen in Australia and Europe.[22,25,28,38]

In 1978, Roberts[49] and, thirty years later, Tóth[69] listed nearly the same reasons for this trend, citing medical staff, pathologists, relatives and hospital management. Physicians and surgeons might think that an autopsy will not provide any more information than has already been found thanks to new diagnostic techniques. Overconfidence in clinical diagnoses due to technical advances is a continuing trend.[28,48,68] However, confidence in a clinical diagnosis is not sufficient assurance of its accuracy and it is impossible to predict whether unexpected findings will arise in an autopsy.[20,38,47] Despite advances in modern medicine, autopsy remains the gold standard for diagnosis.[30]

Inadequate or delayed communication between clinicians and pathologists also sustains declining interest on the part of clinicians. Moreover, fear of a mistake being discovered through an autopsy and possible subsequent malpractice prosecution contribute to clinicians' reluctance,[1,28] even if no increased litigation has been related to high autopsy rates.[58] Furthermore, the desire not to upset the bereaved family and all the necessary red tape restrains physicians from requesting consent for an autopsy.[25]

Pathologists struggle with the lack of recognition that the autopsy sometimes receives and autopsies may be delegated to the pathologist-in-training.[8,28,49,69,72]

The desire among laypersons to leave the body intact and to bury the dead promptly also contribute to families' reluctance to consent to necropsies because of the delay caused by the procedure.[30,54] Furthermore, organ retention scandals have diminished public trust in pathology.[18]

Last but not least, financial constraints and the suspension of minimum autopsy percentages both contribute to the decline in autopsy rates.[16]

In 2003, a review of comprehensive literature showed that the rate of diagnostic errors remains high. The median error rate for misdiagnoses likely to have affected the outcome for the patient was 9% (range 0%-20.7%); and for those involving a principal underlying disease or primary cause of death, it was 23.5% (range 4.1%-49.8%).[57] A second review in 2005 reported discrepant major diagnoses in 15% -

41% of cases. Moreover, it revealed at least one clinically unsuspected finding from autopsy in 45% - 76.5% of the cases.[52] More current studies report major discrepancy rates between 6.0% and 17.2%.[39,42,53,65,66] Most individual studies do not show any significant reduction in discrepancy rates.[4,28,38,52,66,73] This persists even though a large number of new diagnostic techniques have been introduced over the last few decades.[38] The 2003 review showed a decrease in the proportion of misdiagnoses over time, but the error rate was still deemed high enough to encourage the ongoing use of autopsy.[57]

In veterinary medicine autopsy rates show the same declining tendency as in human medicine. Dank et al.[24] reported a significant decrease in the rate of necropsies performed on dogs during 1989, 1999 and 2009 in California. In Switzerland the number of necropsies performed on farm animals, especially cattle and pigs, was nearly halved between 2008 and 2012.[31] This is unexpected considering the lower hurdles in obtaining permission for an animal autopsy compared to that for humans.[37] The relationship between owners and their pets is often similar to that between an individual and his/her own child,[10] which might lead to the same reluctance factors as reported in human medicine. In fact, the reasons for the decline discussed in the veterinary literature are similar to the ones reported in human medicine.[24] Owners may refuse permission due to sentimental, ethical or religious doubts regarding necropsies[24] or simply question the usefulness of the necropsy itself.[74] Among the consequences of declining necropsy rates specifically in veterinary medicine are failure to notice zoonotic diseases and failure to observe emerging diseases, especially rare or uncommon symptoms.[31]

The literature available for comparing clinical and pathological diagnoses in veterinary medicine is sparse. Surveys mostly focus on a restricted question in one species, such as thyroid carcinoma or intracranial neoplasia in dogs,[59,64] gastric ulcers in horses[5] and repeat-breeder syndrome in cows[26], or describe unexpected pathological findings without systematically comparing them with a diagnosis made in vivo.[23,41] Two studies discussing the causes of death in dairy cows focus on the comparison of pre mortem diagnoses made by farmers with necropsy findings.[43,67] To date only three extensive comparative studies without a selection of disease complexes have been made in dogs.[24,37,74]

Errors are not a sole or mandatory result of ignorance or malpractice but also of the necessary fallibility, limitations and errors that are inevitable in applied sciences. To explore the extent of this third factor, detailed records of erroneous diagnoses are needed.[28,29] The aim of the present study was to compare retrospectively clinical and pathological diagnoses in a large number of cats and dogs which had been examined and had undergone necropsy at the animal hospital in Zurich, Switzerland. A thousand cases of each species were included in this study. The occurrence and concurrence of clinical and pathological diagnoses were recorded and compared. The characteristics of each animal and its diagnosis were correlated with the results of the diagnosis comparison and the agreement categories to identify characteristics that had a significant influence on the categories. This was pursued impartially without presuming ignorance or ineptitude on either side.

Material and methods

Study setting

The study was performed as a retrospective investigation at the Vetsuisse Faculty of Zurich. The clinical data were obtained from the Department for Small Animals and the pathological data from the Institute of Veterinary Pathology. Both are teaching and routine diagnostic institutions.

After consultation with a biostatistician it was decided to analyze 1000 cases each for cats and dogs, beginning with the first necropsy case in the year 2004. The period of study for cats extended to 13th June, 2012 (date of death), and for dogs to the 27th January, 2013. The number of cats and dogs that died or were euthanized in the Department for Small Animals during this period was 2840 and 2540, respectively.

The clinical cases were documented in medical histories containing all clinical data, additional examination reports and the documentation of communication between people involved in the case. Necropsy findings were documented in a necropsy report containing the gross findings and, additionally, the histological findings, or further examinations, if done, pathological diagnoses and a commentary. Necropsy data were stored electronically

Inclusion and exclusion criteria

The study included all cats and dogs undergoing at least a full clinical examination and a complete necropsy. In some cases additional examinations such as blood sampling, diagnostic imaging, histologic examination of tissue and/or microbiological testing were performed.
Exclusion criteria were sudden death, abortions, animals that were dead on arrival at the clinic, that died before clinical examination could be performed or that were euthanized without an examination.

Definition of diagnoses

A diagnosis is the determination of the nature of a disease or other problem by examining the patient and recording the symptoms. In this study the diagnosis was defined as the complete syndrome, injury or disease representing the cause of death or euthanasia, the corresponding etiology and consequences. The presence of all these components was no prerequisite for the registration of a diagnosis. For example, acute renal failure with no further specification was accepted as a clinical diagnosis as was tubulonephrosis as a pathological one. If pathology identified an etiology (e.g. oxalate crystals), the over-weighting was acknowledged within the comparison of the diagnoses.
The same procedure was used for consequences. They were attributed to a basic problem if there was a generally accepted link between the two, even if the consequence could in theory have had a cause other than the basic problem (e.g. cardiac failure with lung edema).

Extraction of diagnoses from clinical histories and necropsy reports
Of the 1315 cats and 1421 dogs necropsied during the study period the clinical history or necropsy reports of 239 cats and 297 dogs were missing. The history was untraceable or could not be found because the case-number of the history had not been documented. Of the remaining cases, 76 cats and 124 dogs met an exclusion criterion, resulting in 1000 (76.0%) cats and 1000 (70.4%) dogs that could be analyzed. A qualified veterinarian working on necropsy service reviewed all medical histories and necropsy reports, whereby the necropsy report, apart from the post

mortem request, was scrutinized only after the clinical diagnoses had been defined, in order to prevent influence on the clinical diagnoses. In ambiguous cases a boarded pathologist was consulted and the diagnoses as well as the comparison were discussed and the consensus was registered. In the medical histories the clinical diagnoses had not been documented in a consistent form. Therefore, the clinical diagnoses constituted a synthesis of the clinical history and the request for a necropsy. If a diagnosis was stated in a letter to a referring veterinarian or on the postmortem request, it was judged as valid regardless of other differential diagnoses mentioned in the history, as these are time points when the clinician had to provide a clear statement. Diagnoses and weighted lists of differential diagnoses only noted in the daily clinical records of the case were considered valid if they were in a logical context with the other elements of the clinical history. If there were only unweighted lists of differential diagnoses available or no diagnoses mentioned at all, no diagnosis was registered. The pathological diagnoses were extracted from the diagnosis section of the necropsy reports.

Comparison of diagnoses

In contrast to diagnosis-comparison studies in human medicine, where the occurrence of a clinical and pathological diagnosis is preconditioned, in veterinary medicine there are significant numbers of cases where either only a clinical or a pathological - or no diagnosis at all - was made. Therefore, in a first step, the (co-) occurrence of clinical and pathological diagnoses was compared. There were four possible outcomes: neither clinical nor pathological diagnosis (c-p-), only clinical (c+p-), only pathological (c-p+) or both diagnoses (c+p+). Reasons for the lack of a pathological diagnosis were recorded if there was only a clinical diagnosis available. Possible reasons were: changes in the relevant organs due to autolysis or euthanasia, which hampered the evaluation; damage or loss of the relevant organs; removal of the relevant organs before necropsy by clinicians; impossibility of diagnosing a certain disease by means of pathology; and refutation of the clinical diagnosis without a pathological diagnosis. All cases providing a clinical and a pathological diagnosis were subject to further comparison to assess the agreement level of these diagnoses. In this study, five agreement categories were defined, focusing on the gain of information due to necropsy.

Agreement was used for cases where the clinical and the pathological diagnosis completely concurred. If the totality of pathological findings supported the clinically identified disease, the case was classified as an agreement. Class 3 cases were those with little additional pathological information; for example, the finding or exclusion of metastases, infiltrative growth or a more precise classification of a known neoplasia, or the description or exclusion of other organs affected by a known disease, as well as specification of the extent of a known disease. Class 2 cases were those with moderate benefit, for example, the characterization of an undefined mass or organ failure and the finding or exclusion of consequences of the underlying disease. Class 1 agreement revealed meaningful information, such as the finding or disproving of an etiology, underlying disease or primary neoplasia. If the clinical and pathological diagnosis did not match at all, the case was classified as a disagreement.

Definition of factors possibly influencing the occurrence and agreement of diagnoses

For each animal, additional data - the case attributes - were recorded and correlated with the comparison (occurrence and accordance) of the diagnoses: age, weight, sex, manner of death, the clinical discipline where it was treated, length of time between death and necropsy and quality of the necropsy request. Age was recorded in one-year categories, beginning with one year and strictly counting birthdays. For animals younger than one year, three additional categories: neonatal (up to two weeks), juvenile (two weeks to six months) and juvenile-adult (six months to one year) were defined. For the statistical analysis these categories were coded as 0.02, 0.25 and 0.75 years. The weight was recorded in 0.1 kg steps, rounded off mathematically. Two categories were used for sex, male and female. The information on whether an animal had been neutered was not reliably available and could not be used. For manner of death, natural death and euthanasia where distinguished. *Internal medicine, cardiology, neurology, oncology, reproductive medicine, surgery and other* (*including anesthesia, dermatology, ophthalmology)* were the different clinical disciplinary areas of the Department for Small Animals that sent cases to necropsy. The length of time between death and necropsy was classified into: no day (necropsy performed on the day of death), one day, and two or more days. The quality of the necropsy request was classified as poor (pathologist was not informed

of what the animal was thought to be suffering from clinically) or as good (clinical judgments were stated). If the value of a case characteristic was not available, it was registered as unknown and the case was excluded from statistical analysis for this characteristic.

Similarly, the diagnostic attributes describing the primarily affected organ system and the main disease entity of the clinical diagnosis or of the pathological diagnosis, respectively, were defined and correlated with the comparison of the diagnoses. The organ system categories were *cardiovascular* (heart and vessels), *body cavities* (serosae, mediastinum, mesentery, effusions, and thoracic or abdominal masses that could not be assigned to a specific organ), *digestive* (including exocrine pancreas and liver), *endocrine, exterior* (including skin, adnexa, sensory organs), *immunohematologic, musculoskeletal, neurologic, respiratory, urogenital* (including mammary gland)*, multiple* (multiple clearly-definable organs affected, mainly neoplasia with unknown primary tumor and polytraumas), *systemic* (multiple not-clearly-definable organs affected, mainly systemic infections and septicemia), and *unknown* (cases where the affected organ was unknown, mainly neoplasia of unknown primary tissue). The disease entity categories were *neoplastic, behavioral, congenital, degenerative, genetic, iatrogenic, idiopathic, immune, inflammatory, infectious, metabolic, neurologic, physical* (trauma, radiation), *positional* (compression, displacement, obstruction, rupture), *toxic, vascular and multifactorial* (all diagnoses where different pathophysiological categories were possible, e.g. hypertrophic cardiomyopathy).

Necropsy remains the gold standard for diagnosis[30] and in this study also, the comparison refers to the pathological diagnosis. Therefore, when analyzing the influence of a diagnosis attribute on the occurrence of diagnosis, the attributes of the pathological diagnosis were used in all cases where both or only the pathological diagnosis were/was available. If only a clinical but not a pathological diagnosis was available, the attributes of the clinical diagnosis were subjected to analysis. To assess the influence of a diagnosis attribute on the agreement of diagnoses, the attributes of the pathological diagnosis were used exclusively.

Data collection and statistical analysis

Data were initially collected in a database using the software FileMaker Pro 11

(FileMaker, Inc., USA), and then transferred to Stata Software (StataCorp., 2011; Stata Statistical Software: Release 12; College Station, TX, USA: StataCorp LP) using Excel (Microsoft Inc.). Data editing, calculation of descriptive data and all statistical analyses were done using Stata. To assess the influence of all independent characteristics, except age and weight, on the distribution of occurrence and concurrence categories, a preliminary univariate pearson chi2 test was used. Then age and weight were also tested for possible influence on the outcome of the comparison and as coviariates, using a one-way analysis of variance (ANOVA), including the Bonferroni post hoc test. A P-value of ≤ 0.05 was considered significant. In a second step, a multiple logistic regression (step back procedure according to Altman[2]) was performed, in which characteristics showing a tendency (P-value ≤ 0.2) were entered into the full model. Again, a P-value ≤ 0.05 was considered significant and used as the endpoint in the final model.

Results

Descriptive statistic of case and diagnosis attributes

During the study period, 1315 cats and 1421 dogs that had died or been euthanized at the Department for Small Animals underwent necropsy at the Institute of Veterinary Pathology, resulting in a necropsy rate of 46.3% and 55.9%, respectively. The arithmetic mean age of cats included in the study was 8.8 years (range 0.02 to 21 years). For 54 cats, the age was unknown. In dogs it was 8.2 years (range 0.25 to 26 years), while 38 dogs were of unknown age. The arithmetic mean weight for the cats was 4.1 kg (range <0.5 kg to 11 kg), with no weights missing. For the dogs it was 22.6 kg (range < 0.5kg to 81 kg), with two weights unknown. In all, 407 cats and 485 dogs were female, 557 cats and 509 dogs were male and in 36 cats and 6 dogs the gender was unknown. As for manner of death, 149 cats and 178 dogs had died naturally, while 845 and 814, respectively, were euthanized; in 6 and 8 cases manner of death was not reported. The clinical disciplines from which the animals originated and the number of cases for each discipline are listed in table 1. In both species, the clinical discipline of internal medicine was responsible for the largest number of submissions, followed by neurology. The quality of the post mortem request for cats

was good in 963 cases and poor in 37. For dogs it was good in 969 and poor in 31 cases. There was no delay between death and necropsy (necropsy performed on the day of death) in 231 feline cases, a delay of one day in 547, and of more than one day in 212. In feline 10 cases the delay was not determinable. In dogs no delay was registered in 270, one day in 502 and more than one day in 221 cases. In 7 cases the delay was not determinable. Mean age and weight and number of cases in the other case attribute and occurrence or agreement categories for cats and dogs are shown in the supplemental tables 1 and 2. Numbers of cases in the diagnosis attribute and occurrence or agreement categories for cats and dogs are shown in tables 2 and 3.

Occurrence of diagnoses in cats

In 58 (5.8%) cases neither a clinical nor a pathological (c-p-) diagnosis was made. In 26 (2.6%) cases only a clinical (c+p-) and in 178 (17.8%) only a pathological diagnosis (c-p+) was available. The reasons for the lack of a pathological diagnosis in cases where only a clinical diagnosis was made are listed in table 4. Refutation of the clinical diagnosis without finding a pathological one was by far the most common reason for the absence of a pathological diagnosis. In 738 (73.8%) cases both a clinical and a pathological diagnosis (c+p+) were available.

Regarding the case attributes possibly affecting the distribution of the occurrence of diagnoses, univariate analysis showed a significant influence of manner of death, clinical discipline, and completeness of the necropsy request. Natural death had more effect on distribution than did euthanasia, resulting in fewer c+p+ cases, slightly more c+p- and more c-p+ cases than expected. The outcome of c-p- was not influenced by manner of death. The clinical discipline influencing the number of c+p+ cases the most was neurology, resulting in significantly fewer cases than expected. For c+p- it was cardiology and surgery, both with equal influence, for c-p+ neurology, and for c-p- oncology, all except surgery resulting in more cases than expected. Overall, neurology had the greatest influence on the distribution of occurrence of diagnoses. A poor report had more effect on distribution than a good one, leading to fewer c+p+, and more c+p-, c-p+ and c-p- cases than expected. The univariate analysis of the influence of diagnosis attributes on the distribution of c+p+ and c+p- cases showed an influence caused by the (clinical) organ system and by the disease

entity. ‘Immunohematologic’ was the organ system with the greatest influence on distribution of occurrence; resulting in more c+p- and fewer c+p+ cases; and ‘immune’ was the disease entity with the greatest influence, resulting in more c+p- and fewer c+p+ cases than expected as well. The distribution of c+p+ and c-p+ cases was also influenced by the (pathological) organ system and by the disease entity. The nervous system was the affected organ system with the greatest influence, resulting in more c-p+ and fewer c+p+ cases, and metabolic was the disease entity resulting in more c-p+ and fewer c+p+ cases than expected as well.

The multivariate analysis revealed an influence on the likelihood of occurrence of c+p+ cases by a natural death compared to euthanasia (OR 0.50 (0.34, 0.72)) (point estimation (95% confidence interval)), all clinical disciplines except medicine taken together as opposed to medicine (OR 0.87 (0.81, 0.93)), of which, regarded in isolation, neurology (OR 0.32 (0.21, 0.49)), reproductive medicine (OR 0.42 (0.18, 0.99)) and surgery (OR 0.58 (0.35, 0.94)) were the significantly divergent categories, as well as poor versus good quality of necropsy request (OR 0.58 (0.41, 0.82)). c+p- cases were influenced only by poor versus good request quality (OR 1.90 (1.02, 3.55)). As with the c+p+ cases noted above, c-p+ cases were also influenced by a natural death compared to natural euthanasia (OR 2.27 (1.52, 3.39)), all clinical disciplines except medicine, taken together, as opposed to medicine (OR 1.13 (1.04, 1.22)), of which when analyzed separately neurology (OR 3.16 (2.02, 4.93)) was the only significantly divergent category, and by poor versus good quality post mortem request (OR 1.61 (1.12, 2.33)). c-p- cases were influenced by all clinical disciplines except medicine, taken together, as opposed to medicine (OR 1.18 (1.05, 1.33)), of which oncology (OR 3.96 (1.08, 14.53)) and surgery (OR 2.54 (1.16, 5.55)) were the relevant categories and barely significantly influenced by female compared to male cases (OR 1.77 (1.00, 3.11)).

Accordance of pathological and clinical diagnoses in cats

Of the 738 cases in which a clinical and a pathological diagnosis were available, 283 (38.3%) were in agreement, 127 (17.2%) revealed little (class 3), 109 (14.8%) were moderately of benefit (class 2) and 87 (11.8%) gave meaningful additional information (class 1). Disagreement was found in 132 (17.9%) cases.

Regarding case attributes possibly affecting the distribution of diagnosis agreement,

the univariate analysis showed that manner of death and clinical discipline had a significant influence. Natural death had more effect on distribution than did euthanasia, resulting in more agreement, class 1 and disagreement but fewer class 3 and class 2 agreements than expected. The clinical discipline influencing the number of agreements most was neurology, with fewer cases than expected. Oncology had the greatest influence on class 3, with more cases than expected. Surgery had the greatest influence on class 2, class 1 and disagreement, with fewer class 2 but more class 1 and disagreements than expected. Overall, surgery had the largest influence on the distribution of accordance. Univariate analysis of the influence of diagnosis attributes on the distribution of accordance showed the (pathologic) organ system and disease entity to have an influence. The organ system influencing the classification of agreement most was 'systemic', with more cases than expected. For class 3 it was ‘multiple’ with more, for class 2 'systemic' with fewer, for class 1 genital with more and for disagreement the nervous system, with more cases than expected. Overall the organ system 'systemic' had the greatest influence on distribution. The disease entity influencing the agreement classes 3 and 2 most was neoplastic, with fewer agreements but more class 3 and class 2 cases than expected. ‘Positional’ had the greatest influence on class 1, resulting in more cases than expected, and disagreement was mostly influenced by vascular, with more cases than expected. Overall the disease entity neoplastic had the greatest influence on distribution.

Multivariate analysis revealed the following influences on the odds ratio of the occurrence of agreement: weight (OR 0.89 (0.79, 0.99)); all clinical disciplines except medicine, taken together, as opposed to medicine (OR 0.88 (0.80, 0.96)), of which neurology (OR 0.43 (0.20, 0.91)) was the only significantly divergent category; all organ systems except cardiovascular as opposed to cardiovascular (OR 1.01 (1.00,1.01)), of which the autonomously significant divergent categories were body cavities (OR 11.48 (3.60, 36.57)), digestive tract (OR 2.83 (1.23, 6.49)), endocrine (OR 5.21 (1.94, 14.02)), nervous system (OR 2.96 (1.02, 8.52)), 'systemic' (OR 17.19, (5.24, 56.44)) and urogenital (OR 3.13 (1.43, 6.85)); and by all disease entities except neoplastic as opposed to neoplastic (OR 1.16 (1.12, 1.21)), of which inflammatory (OR 4.78 (2.70, 8.46)), metabolic (OR 5.32 (1.81, 15.66)), multifactorial (OR 5.64 (2.89, 10.99)), toxic (OR 5.28 (1.08, 25.80)) and trauma (OR 3.67 (1.20, 11.24)) were the significantly divergent categories. Class 3 was influenced by the group of all clinical disciplines except medicine as opposed to medicine (OR 1.12

(1.01, 1.24)), of which no discipline was relevant on its own, by all organ systems except cardiovascular as opposed to cardiovascular (OR 0.99 (0.98, 1.00)), of which body cavities (OR 0.17 (0.03, 0.96)), digestive tract (OR 0.29 (0.09, 0.95)), endocrine (OR 0.10 (0.02, 0.48)), immunohematologic (OR 0.08 (0.01, 0.41)), musculoskeletal (OR 0.12 (0.02, 0.72)), nervous system (OR 0.21 (0.05, 0.85)), respiratory (OR 0.29 (0.09, 0.99)) and urogenital (OR 0.17 (0.05, 0.61)) were the divergent categories, and by the group of all disease entities except neoplastic as opposed to neoplastic (OR 0.82 (0.78, 0.86)), whereby the autonomously divergent categories were inflammatory (OR 0.08 (0.03, 0.23)), infectious (OR 0.05 (0.01, 0.40)), and multifactorial (OR 0.15 (0.05, 0.44)). Class 2 was influenced by a natural death compared to euthanasia (OR 0.24 (0.08, 0.80)) and by all disease entities except neoplastic taken together as opposed to neoplastic (OR 0.87 (0.83, 0.91)), whereby again inflammatory (OR 0.49 (0.27, 0.89)), infectious (OR 0.06 (0.01, 0.23)) and multifactorial (OR 0.35 (0.18, 0.68)) were the divergent categories. Class 1 was influenced only by a natural death versus euthanasia (OR 2.11 (1.19, 3.75)). Disagreement was influenced by all clinical disciplines except medicine, taken together, as opposed to medicine (OR 1.11 (1.01, 1.21)), whereby no clinical discipline was relevant on its own, and by the group of all disease entities except neoplastic as opposed to neoplastic (OR 1.08 (1.03, 1.12)), of which idiopathic (OR 7.10 (1.66, 30.40)), inflammatory (OR 2.27 (1.29, 4.02)), infectious (OR 1.93 (1.08, 3.45)) and multifactorial (OR 10.37 (2.73, 39.34)) were the divergent categories.

Occurrence of diagnoses in dogs

In 52 (5.2%) cases neither a clinical nor a pathological diagnosis was made. In 38 (3.8%) cases only a clinical and in 112 (11.2%) only a pathological diagnosis was available. The reasons for the absence of a pathological diagnosis in cases where only a clinical diagnosis was made are listed in table 4. As with the cats, the refutation of a clinical diagnosis without finding a pathological diagnosis was the most common reason for a missing pathological diagnosis. Additionally, the impossibility of diagnosing the clinical disease by means of pathology was a weighty cause. In 798 (79.8%) cases a clinical and a pathological diagnosis were available. The distribution of occurrence of diagnoses in dogs showed a significant difference to the distribution in cats.

Regarding case attributes possibly affecting the distribution of the occurrence of diagnoses, univariate analysis showed a significant influence of manner of death and clinical discipline. Completeness of post mortem request (p=0.051) marginally missed the significance level. A natural death had more effect on distribution than did euthanasia, resulting in fewer c+p+ cases, slightly more c+p- and more c-p+ than expected. Manner of death made no difference to the outcome of c-p- cases. The clinical discipline influencing the number of c+p+ most was surgery, with fewer cases than expected. For c+p- it was oncology, with fewer cases than expected; for c-p+ it was again surgery, with more cases, and for c-p- it was neurology, also with more cases than expected. Overall, surgery had the greatest influence on the distribution of occurrence. Univariate analysis of the influence of diagnosis attributes for the distribution of c+p+ and c+p- cases only showed an influence on the part of the (clinical) disease entity, with neurological diseases having the greatest influence, resulting in more c+p- cases and fewer c+p+ cases than expected. The distribution of c+p+ and c-p+ cases was influenced only by the (pathologic) organ system, with the nervous system having the greatest influence and resulting in more c-p+ and fewer c+p+ cases than expected.

Multivariate analysis revealed an influence on the likelihood of occurrence of c+p+ of a natural death as compared to euthanasia (OR 0.49 (0.30, 0.78)), of all clinical disciplines except medicine as opposed to medicine (OR 0.81 (0.74, 0.88)), whereby when analyzed separately, neurology (OR 0.28 (0.16, 0.49)), reproductive medicine (OR 0.26 (0.08, 0.83)) and surgery (OR 0.29 (0.15, 0.53)) were the significantly divergent categories, of a delay between death and necropsy as opposed to no delay (OR 0.84 (0.72, 0.98)), whereby only a delay of two and more days (OR 0.50 (0.27, 0.91)) was relevant, and of all (pathologic) disease entities except neoplastic together as opposed to neoplastic (OR 0.93 (0.89, 0.97)), whereby inflammatory (OR 0.51 (0.27, 0.98)) and multifactorial (OR 0.42 (0.21, 0.83)) were the divergent categories. c+p- cases were not influenced by any characteristic. c-p+ cases, like c+p+ cases, were influenced by a natural death as compared to euthanasia (OR 2.05 (1.28, 3.29)), all clinical disciplines except medicine as opposed to medicine (OR 1.23 (1.13, 1.35)), of which neurology (OR 3.60 (2.05, 6.29)), reproductive medicine (OR 3.81 (1.20, 12.04)) and surgery (OR 3.48 (1.87, 6.46)) were the autonomously divergent categories, by a delay between death and necropsy as opposed to none (OR 1.19 (1.02, 1.38)), whereby only a delay of two and more days (OR 2.00 (1.10,

3.66)) was relevant, and by all disease entities except neoplastic as opposed to neoplastic (OR 1.08 (1.03, 1.13)), whereby inflammatory (OR 1.96 (1.03, 3.75)) and multifactorial (OR 2.40 (1.20, 4.82)) were again the divergent categories. c-p- cases were influenced only by all clinical disciplines except medicine as opposed to medicine (OR 1.22 (1.09, 1.37)), whereby neurology (OR 2.88 (1.47, 5.67)), reproductive medicine (OR 4.62 (1.27, 16.79)) and surgery (OR 2.80 (1.26, 6.24)) were the divergent categories.

Agreement of pathological and clinical diagnoses in dogs

Of the 798 cases in which both a clinical and a pathological diagnosis were available, 289 (36.2%) were in agreement, while 213 (26.7%) cases showed a class 3, 89 (11.2%) a class 2 and 79 (9.9%) a class 1 discrepancy. Disagreement was found in 128 (16.0%) cases. This distribution of diagnosis agreement in dogs showed a significant difference to that in cats.

Regarding the case attributes possibly affecting the distribution of diagnosis agreement, univariate analysis showed a significant influence of weight only. The mean weight of dogs in class 3 was significantly higher than in the categories agreement, class 2, class 1 and disagreement. Univariate analysis of the influence of diagnosis attributes on the distribution of agreement showed influences of the organ system and of disease entity. The organ system most influencing the number of agreement, class 3, and disagreement groups was 'multiple', with many more cases in class 3, but fewer than expected in others. For class 2 it was sensory and for class 1 digestive, both with more cases than expected. Overall, 'multiple' had by far the greatest influence on the distribution of agreements. Neoplastic was the disease entity primarily influencing the number of agreement, class 3, class 2 and disagreement groups, with fewer agreements and disagreements but more class 3 and class 2 than expected. Degenerative had the greatest influence on class 1, resulting in more cases than expected. Overall, neoplastic had the greatest influence on the distribution of agreement.

Multivariate analysis revealed a significant influence on the odds ratio of the occurrence of agreement of the following factors: weight (OR 0.99 (0.98, 1.00)) and the group of all disease entities except neoplastic as opposed to neoplastic alone (OR 1.13 (1.09,1.17)), whereby congenital (OR 15.14 (4.71, 48.70)), genetic (OR

18.18 (1.99, 165.66)), idiopathic (OR 4.55 (1.81, 11.44)), immune (OR 20.06 (5.55, 72.53)), inflammatory (OR 5.36 (3.31, 8.68)), infectious (OR 6.42 (3.83, 10.74)), multifactorial (OR 3.06 (1.81, 5.18)) and positional (OR 4.62 (2.04, 10.45)) were the autonomously divergent categories. Class 3 was influenced by weight (OR 1.02 (1.00, 1.03)), by all organ systems except cardiovascular as opposed to cardiovascular alone (OR 1.01 (1.00, 1.02)), whereby 'multiple' analyzed separately (OR 4.86 (1.93, 12.24)) was the only divergent category, and by all disease entities except neoplastic as opposed to neoplastic (OR 0.74 (0.69, 0.78)), whereby degenerative (OR 0.29 (0.10, 0.83)), idiopathic (OR 0.06 (0.01, 0.45)), inflammatory (OR 0.04 (0.01, 0.12)), infectious (OR 0.06 (0.01, 0.26)), multifactorial (OR 0.13 (0.06, 0.31)) and positional (OR 0.10 (0.02, 0.46)) were the divergent categories. Class 2 was influenced only by the group of all disease entities except neoplastic as opposed to neoplastic (OR 0.94 (0.89, 0.99)), whereby the only autonomously divergent category was infectious (OR 0.20 (0.06, 0.65)). Class 1 was not influenced by any characteristic. Disagreement was influenced only by the group of all disease entities except neoplastic as opposed to neoplastic (OR 1.12 (1.07, 1.17)), whereby degenerative (OR 4.13 (1.87, 9.04)), inflammatory (OR 4.36 (2.43, 7.83)), infectious (OR 2.67 (1.37, 5.21)), multifactorial (OR 5.26 (2.85, 9.71)), positional (OR 3.60 (1.33, 9.72)), and vascular (OR 8.40 (2.96, 23.83)) were the divergent categories.

Discussion

This study compared clinical and pathological diagnoses linked with mortality in cats and dogs with respect to the occurrence and agreement of diagnoses using pathology as the gold standard. Case and diagnosis related attributes were analyzed for a possible influence on occurrence and agreement of diagnoses.

The scheme for comparison of diagnoses in the present study, focusing on the gain of information due to necropsy, differs slightly from that commonly used in human medicine. Goldman proposed a classification for the comparison of diagnoses in 1983[28] that has been modified by Battle[7] and used in numerous studies for the comparison of diagnoses in human medicine.[42,44,46,51,60,66,68,71] This classification is based on the question of whether knowledge of the discrepancy would have led to a change in patient management or survival. In animals, especially in a retrospective

study, the question of change in management and survival cannot be answered precisely, as it is dependent on veterinary medicine in particular and also on pathologist-practitioner-owner interaction, which needs to consider questions such as economic constraints and owner attitude. Actually, the few studies comparing diagnoses in veterinary medicine do not use management and survival as a classifying category and distinguish only between single or further specified, total agreement and disagreement.[24,37,74] Only as an additional question did Vos et al. investigate the clinical relevance of discrepancies.[74]

The necropsy rate of 46.3% in cats and 55.9% in dogs in the present study was similar to or, considering the time frame of the studies, even higher than that reported in dogs by Kent and Dank[24,37] and clearly above the range in human medicine.[42,45,54,66,68] Certainly it exceeded the minimal rate of 15% to 35% recommended in human medicine[6,11,40] but was below the 100% rate for a fully effective quality assessment of diagnostic accuracy.[3,32.] The slightly higher necropsy rate in dogs as compared to cats might reflect the possibly higher esteem in which individual animals were held and therefore the effort made to find the cause of death.
A substantial percentage of cases, 18.2% in cats and 20.9% in dogs, that had undergone necropsy could not be included in the study because some of the required data (clinical history and or necropsy report) were missing by pure chance and did not influence the outcome of the study. Another potential impact on results and potential criticism of the study might stem from the fact that the comparison was conducted by pathologists, however, it has been shown that the type and level of discrepancy was virtually the same regardless of the background (clinician or pathologist) of the assessing persons.[7]

In 5.8% of the cats and 5.2% of the dogs neither a clinical nor a pathological diagnosis was made, and in 17.8% and 11.2%, respectively, only a pathological diagnosis. This leads to 75.4% (cats) and 68.3% (dogs) of clinically unsolved cases that could be worked out by pathology, providing a clear benefit to all parties interested in a certain case. It should be kept in mind that only cases that had undergone a clinical examination were included in the present study. If cases of sudden death had been integrated, the percentage of diagnoses revealed at necropsy might have been even higher, as a study in dogs that had died during

grooming procedures indicates.[41] In the only veterinary study to analyze the occurrence of diagnoses, Voss et al. found at least a clinical or a pathological diagnosis in all cases, of which only a pathological one was found in 4.1% of the cases.[74]

The percentage of cases where only a clinical diagnosis was made (2.6% (n=26) in cats and 3.8% (n=38) in dogs) was fairly small and much smaller than the 13.8% reported by Vos et al.[74] Euthanasia artifacts, damage, loss or failure to examine relevant organs and the removal of relevant organs before necropsy were sporadic reasons for missing pathological diagnoses. With regard to quality assessment of medicine through pathological diagnoses, these avoidable failures should be taken seriously and avoided in future regardless of their small number. In four cats and twelve dogs clinical diagnosis was impossible to confirm by means of pathology, a clear limit of necropsy as a quality assessment tool. The most common examples were babesiosis, detrusor-urethral dyssynergia and tetanus.

Both diagnoses were available in 73.3% of cats and 79.8% of dogs. By way of comparison, Vos et al. reported 82% in dogs.[74] The significantly smaller percentage in cats might again be due to the tendency for an individual animal to be held in lower esteem as compared to a dog or to a potentially more difficult clinical examination in cats. The lower necropsy rate and the significantly higher percentage of cases lacking a clinical but not a pathological diagnosis in cats versus dogs underline this hypothesis. Once the decision for a necropsy has been made, costs were no longer a limiting factor as for the time period and institution where this study was performed the necropsy service was, apart from exceptional cases, financed by the Institute of Pathology.

Of all cases exhibiting both a clinical and a pathological diagnosis, disagreement was found in 17.9% of cats and 16.0% of dogs. When taking into account the 15 (cat) and 14 (dog) cases for which no pathological diagnosis was made but for which the clinical diagnosis was disproved, also implying disagreement, these percentages would hypothetically be roughly two percentage points higher. One prospective study analyzing 145 dogs in 2005 found 26.0% of disagreeing diagnoses.[74] Another retrospective study analyzing 339 and 284 dogs in 1989 and 1999, respectively, as well as the follow up study including 148 dogs in 2009 reported disagreement in 39.8%, 37.0% and 14.9% of cases, whereby the decline from 37.0% to 14.9% proved

to be significant.[24,37] The discrepancy rate in the present study for both species is at the bottom end of the scale defined by previous studies. This might well be due to the fact that data were derived from a teaching hospital, where cases can be evaluated particularly extensively, as postulated by Dank et al.[24] Analogies to human medicine, where the range of error rates for misdiagnoses involving principal underlying disease or primary cause of death was 4.1% to 49.8%, with a tendency to decline over time also,[52,57] should be made with caution, as the classification of agreement differs substantially among the various studies.

Total agreement was found in 38.3% of cats and 36.2% of dogs. In comparable studies this rate was between 51.3% and 85.1%[24,37,74] and in human medicine between 45% and 88%.[14,46] It was reported that necropsy is requested more often when diagnostic uncertainty exists, thereby - and especially if the necropsy rate was low - shifting the results of the comparison towards disagreements.[37,46,56] However, earlier studies in both disciplines showed that there was no difference between consecutive and nonconsecutive submissions,[20,21,74] that no level of clinical diagnostic certainty could predict the pathological findings[47] and, even in clinically fairly certain cases, that the main diagnosis was correct in only 75% of cases, raising the authors' doubts that a clinician is always well placed to judge the potential value of a necropsy.[20] The significantly higher discrepancy rate in cats versus dogs may again be due to the potentially lower effort made to find a clinical diagnosis in cats, or there may be species differences in disease presentation.[24]

A discrepancy but no complete disagreement between the clinical and pathological diagnosis was found in 43.8% of cats and 47.8% of dogs, whereas 22.7% discrepancies were found in the only available veterinary medicine study respecting discrepancies.[74] In comparison to previous studies using either no or broad categories, the present study used a detailed graduation of discrepancies, classifying all cases with a small amount of additional information gained from necropsy as class 3 discrepancy. This is the likely cause of the relatively higher discrepancy or lower agreement rate than in other studies.[24,37,74] In cats, slightly more class 3 (little) than class 2 (moderate) and class 1 (meaningful) discrepancies were found, whereas in dogs class 3 was overrepresented. As this finding indicates more detailed clinical diagnoses in dogs, it might again be due to the potentially higher diagnostic effort invested in dogs.

Investigation of potential causes of discrepancies between clinical and pathological diagnoses is indicated in view of quality assessment and particularly in view of quality improvement with respect to patient care.[70]

In the univariate analysis of case related attributes age, weight and sex of the animal and length of time between death and necropsy in both species had no influence on the occurrence of a clinical or pathological diagnosis. In contrast, a natural death led to relatively more cases with a missing clinical diagnosis. According to Cabot, clinicians are more likely to fail to diagnose terminal lesions,[19] a fact which is supported by the findings in this study. Moreover, veterinary doctors may be more reluctant to euthanize an animal if no diagnosis has been made. The quality of the post mortem request only significantly influenced the occurrence of diagnoses in cats, but showed the same tendency in dogs. It is striking that, if a clinical diagnosis was known, a poor request led to the high likelihood of a missing pathological diagnosis, a fact emphasizing that there must be collaboration between clinicians and pathologists before the autopsy[33] to enhance the quality of pathological diagnoses. The influence of the request if no clinical diagnosis was made is biased through the fact that a clinician cannot, without a diagnosis or suspicion thereof, provide a good quality request according to the definition of this study and this should not therefore be interpreted. The clinical discipline where the animal had been treated did affect the occurrence of diagnoses in both species. The influence of the different disciplines among the occurrence categories and species, even if neurology and surgery proved to have the greatest, is highly variable and the reason for this influence should be the subject of further investigation. In cats, while the organ system affected by the clinical or pathological diagnosis and the disease entity characterizing it did influence the occurrence of diagnoses, in dogs, the organ system influenced the occurrence of a pathological diagnosis and the disease entity the occurrence of a clinical diagnosis only.

When all different potential influence factors were played off against each other in a multivariate analysis, in cats only manner of death (influencing the occurrence of c+p+ and c-p+), clinical discipline (influencing c+p+, c-p+ and c-p-) and quality of post mortem request (influencing c+p+, c+p- and c-p-) remained significant. Additionally, sex appeared to have an influence on the occurrence of c-p-. A plausible explanation for this cannot be found except as statistical chance reflected in a confidence interval practically including one. In dogs, manner of death (influencing

the occurrence of c+p+ and c-p+) and clinical discipline (influencing c+p+, c-p+ and c-p-) remained significant. Additionally, a delay of two and more days between death and necropsy halved the chance of having both (clinical and pathological) diagnoses. On average, dogs are heavier and have thicker coats than cats and in the authors' experience more subject to autolysis. A hypothesis supported by the fact that only in dogs did autolysis hamper the necropsy (in four cases). Therefore to enhance the quality of pathological diagnoses, especially in dogs, a prompt necropsy is required. The disease entity of the pathological diagnosis, occurring as a significant influence factor only in the multivariate analysis (on c+p+ and c-p+), is not thought to be of great impact, because in both cases it had an OR close to one.
To summarize, even if, when analyzed separately, there were attributes of the case and diagnosis that influenced the occurrence of diagnosis, multivariate analysis revealed that only case associated attributes were of relevance in both species.

Regarding agreement of the clinical and pathological diagnoses, the univariate and the multivariate analysis showed an influence of the diagnosis attributes organ system and disease entity for both species. 'Systemic' in cats, leading to more total agreements but fewer class 2 disagreements, and 'multiple' in dogs, leading to fewer agreements and disagreements but more class 3 discrepancies, were the organ systems showing the greatest influence. This is not surprising if one considers that systemic diseases, once a diagnosis is made, can be precisely defined. In contrast, diseases with the involvement of multiple organs are potentially more accurately described through necropsy. That the most influential factor in cats was 'systemic' while it was 'multiple' in dogs might be due to the correspondingly higher number of cases in these categories and thereby higher statistical potential. A striking result is that in both species the disease entity most influencing agreement was 'neoplastic', which resulted in fewer agreements but more class 3 and class 2 discrepancies and, in dogs, more disagreements as well. Even though discrepancies between clinical and pathological diagnoses in neoplastic diseases have been reported to be of little value from a teaching standpoint[33,35], the present finding indicates a clear benefit through a more precise diagnosis by necropsy, especially in neoplastic disease.
Of the case related attributes, in cats manner of death and clinical discipline in the uni- and multivariate analysis, and weight in the multivariate revealed an influence on agreement between the diagnoses. As discussed, for occurrence of diagnoses, the

influence of the different disciplines on agreement is highly variable and the reason for this should also be subject to further investigation. In dogs, the only case related attribute in the uni- and the multivariate analysis showing an influence on agreement was weight. It led to a lower risk of agreement the heavier the animal was; the same was true in cats. The reason for this is unclear. As for the occurrence of diagnoses, the univariate analysis showed no influence of the case related attributes age, weight and sex of the animal and length of time between death and necropsy on agreement of the clinical and pathological diagnosis in either species. Additionally, the quality of the necropsy request did not influence agreement and, in dogs only, clinical discipline also had no influence.

To summarize, in contrast to the occurrence of diagnoses, the main influence on their agreement were the diagnosis related attributes. Case related attributes were only rarely of significance.

As in human medicine, significant progress in diagnostic procedures has been made over the last decades.[37] Further prospective studies need to be done to assess the value of the various clinical diagnostic tools such as diagnostic imaging or, particularly interesting from a pathologist's point of view, biopsy. On the pathology side, it should be assessed whether further diagnostics such as immunohistology or special stains have an influence on the occurrence and agreement of diagnoses.

Conclusion

Even if the rate of discrepancies between the clinical and the pathological diagnosis in the present study was rather low compared to other studies, the high rate of discrepancies clearly shows that necropsy provides valuable additional information in nearly 50% of cases. Of these, about a third were meaningful, as they revealed or disproved an etiology or the primary underlying disease. And, especially in neoplastic diseases, necropsy is capable of defining the disease more precisely. In human medicine, about half of the cases were also found to be of probable educational value.[35] If no clinical diagnosis could be made at all, necropsy was able to reveal the cause of death in about three quarters of cases. The data at hand underscores the lasting value of necropsy as a tool in unveiling unclear cases, in quality monitoring

and, through refining diagnoses, in teaching, especially in species in which a clinical diagnosis might be hampered, or where an animal died of natural causes.

To derive the most from a necropsy, importance must be attached to the case related attributes. Intensive collaboration between clinicians and pathologists must be striven for and the necropsy should be performed without delay after death. The importance of necropsies does not lie in pure numbers, and pathologists should devote less time to performing autopsies of questionable clinical research or educational value.[14,33] As the accordance between diagnoses was dependent mainly on the affected organ or disease entity of the diagnosis, further research should be undertaken on this topic. Organ systems and disease entities promising a great benefit through necropsy need to be identified precisely. This will help to selectively choose cases for necropsy, thus saving resources, which is an issue of increasing importance, and to keep alive the continuing value of the necropsy in veterinary medicine.

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Table 1. Number of cases broken down by the examining clinical disciplines.

clinical discipline	cats (n=1000)	dogs (n=1000)
medicine	707	660
cardiology	27	20
neurology	115	159
oncology	19	25
reproductive medicine	23	21
surgery	86	98
other*	10	7
unknown	13	10

* includes anesthesia, dermatology and ophthalmology.

Table 2. Number of cases in the clinical and pathological diagnosis attribute and occurrence categories for cats and dogs.

	cats				dogs			
	clinical		pathological		clinical		pathological	
	c+p+	c+p-	c+p+	c-p+	c+p+	c+p-	c+p+	c-p+
organ system								
cardiovascular	71	6	76	24	60	1	67	11
body cavities	80	1	30	2	51	0	21	1
digestive	114	2	111	29	138	5	130	15
endocrine	35	1	36	5	24	4	27	4
exterior	14	0	11	1	15	0	12	0
immunohematologic	31	4	28	3	77	5	52	5
musculoskeletal	16	1	17	1	32	2	41	5
neurologic	51	4	53	39	94	8	88	37
respiratory	86	1	97	18	80	4	62	9
urogenital	124	1	117	10	90	5	104	6
multiple	19	1	72	17	78	1	145	9
systemic	80	2	88	29	46	2	49	10
unknown	17	2	2	0	13	1	0	0
disease entity								
neoplastic	218	5	276	52	325	11	351	34
behavioral	0	0	0	0	0	1	0	0
congenital	10	2	11	0	22	3	18	2
degenerative	1	0	6	3	20	1	43	5
genetic	3	0	6	2	7	0	5	0
iatrogenic	1	0	1	0	3	0	6	0
idiopathic	9	2	8	1	21	0	20	1
immune	13	3	3	0	31	2	16	3
inflammatory	39	2	119	19	57	2	105	20
infectious	122	6	121	40	88	6	88	18
metabolic	15	1	17	14	2	0	3	2
neurologic	0	0	0	0	3	3	0	0
physical	19	0	20	4	13	1	13	4
positional	26	1	12	2	25	1	26	2
toxic	6	1	8	0	6	1	5	0
vascular	8	0	10	6	23	0	17	5
multifactorial	248	3	120	35	152	6	82	16

Abbreviations: c+p+, clinical and pathological diagnosis available; c+p-, only clinical diagnosis available; c-p+, only pathological diagnosis available.

Table 3. Number of cases in the (pathological) diagnosis attribute and agreement categories for cats and dogs.

	cats						dogs					
	agree	class 3	class 2	class 1	disag	**total**	agree	class 3	class 2	class 1	disag	**total**
organ system												
cardiovascular	23	17	5	10	21	**76**	29	9	5	8	16	**67**
body cavities	18	4	0	4	4	**30**	7	5	5	2	2	**21**
digestive	42	18	18	15	18	**111**	48	23	15	21	23	**130**
endocrine	19	3	8	3	3	**36**	9	7	5	4	2	**27**
exterior	2	3	3	0	3	**11**	3	5	2	0	2	**12**
immunohematologic	6	3	8	4	7	**28**	24	5	7	6	10	**52**
musculoskeletal	4	3	5	3	2	**17**	20	4	6	5	6	**41**
neurologic	14	10	6	3	20	**53**	32	29	5	5	17	**88**
respiratory	20	23	19	14	21	**97**	25	10	7	2	18	**62**
urogenital	59	8	23	20	7	**117**	41	15	17	13	18	**104**
multiple	10	34	13	5	10	**72**	15	101	15	6	8	**145**
systemic	65	0	1	6	16	**88**	36	0	0	7	6	**49**
unknown	1	1	0	0	0	**2**	0	0	0	0	0	**0**
disease entity												
neoplastic	50	96	70	27	33	**276**	62	185	53	24	27	**351**
behavioral	0	0	0	0	0	**0**	0	0	0	0	0	**0**
congenital	3	4	1	2	1	**11**	14	2	1	0	1	**18**
degenerative	2	0	1	3	0	**6**	12	5	3	12	11	**43**
genetic	1	1	1	3	0	**6**	4	0	1	0	0	**5**
iatrogenic	0	0	1	0	0	**1**	2	0	0	3	1	**6**
idiopathic	2	0	0	2	4	**8**	10	1	2	3	4	**20**
immune	2	0	0	0	1	**3**	13	1	0	1	1	**16**
inflammatory	63	5	16	8	27	**119**	57	3	14	3	28	**105**
infectious	76	1	2	16	26	**121**	51	2	3	16	16	**88**
metabolic	9	0	1	4	3	**17**	2	0	0	0	1	**3**
neurologic	0	0	0	0	0	**0**	0	0	0	0	0	**0**
physical	7	4	1	3	5	**20**	5	2	2	4	0	**13**
positional	2	0	2	6	2	**12**	13	2	1	4	6	**26**
toxic	5	0	0	1	2	**8**	5	0	0	0	0	**5**
vascular	2	1	0	1	6	**10**	6	3	1	0	7	**17**
multifactorial	59	15	13	11	22	**120**	33	7	8	9	25	**82**

Abbreviations: agree, agreement; class 3, little additional information; class 2, moderate additional information; class 1, meaningful additional information; disag, disagreement.

Table 4. Reasons for absence of a pathological diagnosis in cases
where only a clinical diagnosis was done.

reason	cats	dogs
autolysis hampered evaluation	0	4
euthanasia hampered evalutation	1	0
damage or loss of relevant organs	5	7
removal of relevant organs before necropsy	1	1
impossible to diagnose by means of pathology	4	12
refuting the clinical diagnosis	15	14

Supplemental Table 1. Mean respectively numbers of cases in the case attribute and occurrence categories for cats and dogs.

	cats					dogs				
	c+p+	c+p-	c-p+	c-p-	**total**	c+p+	c+p-	c-p+	c-p-	**total**
age (mean)	8.8	6.4	8.9	8.5	**8.8**	8.0	8.3	9.0	9.0	**8.2**
weight (mean)	4.1	4.1	3.9	4.1	**4.1**	23.1	23.2	19.4	21.1	**22.6**
sex (n)										
male	416	13	104	24	**557**	405	22	60	22	**509**
female	301	12	65	29	**407**	390	16	51	28	**485**
manner of death (n)										
natural	89	5	46	9	**149**	122	9	38	9	**178**
euthanasia	644	21	131	49	**845**	669	29	73	43	**814**
clinical discipline (n)										
medicine	550	19	105	33	**707**	562	24	51	23	**660**
cardiology	24	2	1	0	**27**	17	1	2	0	**20**
neurology	63	4	39	9	**115**	111	6	27	15	**159**
oncology	15	0	0	4	**19**	24	0	0	1	**25**
reproductive medicine	13	1	7	2	**23**	13	0	5	3	**21**
surgery	56	0	21	9	**86**	62	5	22	9	**98**
other	6	0	4	0	**10**	5	0	1	1	**7**
delay death-necropsy (n)										
no	167	5	46	13	**231**	221	8	24	17	**270**
one day	409	16	95	27	**547**	406	20	53	23	**502**
two and more days	155	5	36	16	**212**	164	10	35	12	**221**
quality of request (n)										
good	719	23	166	55	**963**	778	35	105	51	**969**
poor	19	3	12	3	**37**	20	3	7	1	**31**

Abbreviations: c+p+, clinical and pathological diagnosis available; c+p-, only clinical diagnosis available; c-p+, only pathological diagnosis available; c-p- neither clinical nor pathological diagnosis available.

Supplemental Table 2. Mean or numbers of cases in the case attribute and agreement categories for cats and dogs.

	cats						dogs					
	agree	class 3	class 2	class 1	disag	**total**	agree	class 3	class 2	class 1	disag	**total**
age (mean)	8.3	9.6	9.0	9.1	8.9	**8.8**	7.7	8.0	8.5	8.4	8.3	**8.4**
weight (mean)	4.0	4.3	4.2	4.2	4.2	**4.1**	20.7	27.2	22.3	23.2	22.1	**22.6**
sex (N)												
male	164	74	58	43	77	**416**	139	112	46	40	68	**405**
female	114	50	49	40	48	**301**	147	101	43	39	60	**390**
manner of death (N)												
natural	38	10	3	18	20	**89**	51	21	14	12	24	**122**
euthanasia	243	116	105	69	111	**644**	234	190	75	67	103	**669**
clinical discipline (N)												
medicine	222	88	86	66	88	**550**	204	141	69	57	91	**562**
cardiology	8	3	6	2	5	**24**	5	7	3	0	2	**17**
neurology	17	11	13	6	16	**63**	41	38	9	8	15	**111**
oncology	4	6	2	0	3	**15**	5	13	2	1	3	**24**
reproductive medicine	6	3	0	2	2	**13**	8	1	1	1	2	**13**
surgery	17	12	1	11	15	**56**	23	11	5	11	12	**62**
other	1	2	1	0	2	**6**	3	1	0	0	1	**5**
delay death-necropsy (N)												
no	62	28	28	14	35	**167**	81	49	25	26	40	**221**
one day	147	75	63	50	74	**409**	143	124	47	38	54	**406**
two and more days	71	24	17	22	21	**155**	63	38	17	14	32	**164**
quality of request (N)												
good	276	127	105	83	128	**719**	284	207	85	77	125	**778**
poor	7	0	4	4	4	**19**	5	6	4	2	3	**20**

Abbreviations: agree, agreement; class 3, little additional information; class 2, moderate additional information; class 1, meaningful additional information; disag, disagreement.

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Curriculum Vitae

Vorname Name	Therese Irene Schertenleib
Geburtsdatum	28/01/1987
Geburtsort	Schlieren
Nationalität	Schweiz
Heimatort	Vechigen BE
Monat/Jahr – Monat/Jahr	**Schulausbildung** (Schulbezeichnung, Ort, Land)
August/1999 – August/2005	Kantonsschule Zürcher Oberland, Wetzikon, Schweiz
August/1993 – August/1999	Primarschule Bühl, Wetzikon, Schweiz
Datum	**Höchster Schulabschluss** (Matura etc., Schule, Ort, Land)
30/08/2005	Matura, Kantonsschule Zürcher Oberland, Wetzikon, Schweiz
Monat/Jahr – Monat/Jahr	**Studium** (Fachgebiet, Universität, Ort, Land)
September/2006 – Januar/2013	Veterinärmedizin, Universität Zürich, Zürich, Schweiz
Datum	Abschlussprüfung vet. med. (Universität, Ort, Land)
23/01/2013	Universität Zürich, Zürich, Schweiz
Mt./Jahr – Mt./Jahr	Anfertigung der Dissertation
März/2013 – Februar/2015	Unter Leitung von Prof. em. Dr. Andreas Pospischil, ehemaliger Direktor des Instituts für Pathologie Vetsuisse-Fakultät Universität Zürich, Schweiz
	Alle fachrelevanten Anstellungen nach Abschluss des veterinärmedizinischen Studiums bis zum Einreichen der Dissertation in chronologischer Reihenfolge
Mt./Jahr – Mt./Jahr	Position/Stellung, Institution, Ort, Land
März/2013 – Feburar/2015	Doktorandin/Assistentin, Institut für Veterinärpathologie, Zürich, Schweiz
April/2015 – unbefristet	Amtstierärztin, Veterinäramt der Urkantone, Brunnen, Schweiz